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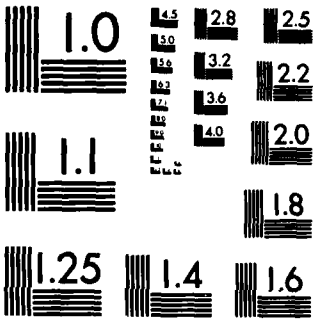

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Sequential Morphologic Alterations in the Foveola and Cornea of Nonhuman Subjects After Exposure to Coherent Light

Annual Progress Report

William H. Spencer, M. D.

March 1984

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TABLE OF CONTENTS

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REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

This is an investigation of the sequential, clinical and morphologic (light and electron microscopic) effects upon the retina of single, short duration pulses of coherent light at 694.3 nm and 532 nm. Also being studied are the effects upon the cornea of coherent light at 10.6 microns (assessed by scanning electron microscopy). The baseline study is to be followed by a similar investigation of the effects of systemic non-steroidal, anti-inflammatory agents upon the extent of the laser induced lesions. Progress has been delayed by recent

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modifications in regulations pertaining to the use of animals for research purposes. An animal use protocol has now been approved by appropriate officials at the Letterman Army Institute of Research and permission has been granted to proceed with the investigation.

ORIGINATOR-SUPPLIED KEYWORDS:

FORM 1473.

SUMMARY

This investigation of the parameters of the damaging effects of coherent light upon the primate retina was initiated because of concern that the eyes of military or civilian personnel might inadvertently be exposed to this form of energy causing transient or permanent visual loss. The effects of coherent light upon ocular tissues are known to vary with the physical characteristics of the energy exposure (wavelength, duration of pulse, spot size, amplitude). This study examines the morphologic effects upon the retina of coherent light at two different wavelengths identical to those used in military devices, and also examines the effects of coherent light in the infrared range upon the cornea. The study is also concerned with the possibility of favorably altering the effects of tissue damage by use of non-steroidal, anti-inflammatory medications. The investigation has been delayed by modifications and regulations pertaining to the use of animals for research purposes. The work is now proceeding but insufficient data has been accumulated to permit conclusions and/or recommendations to be drawn.

FOREWORD

In conducting the research described in this report the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals" prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (DHEW Publication No. (NIH) 78-23, Revised 1978).

REPORT

This is a report of an investigation performed at the Eye Pathology Laboratory of the Pacific Presbyterian Medical Center (PPMC) as a joint effort with personnel of the Division of Biorheology at the Letterman Army Institute of Research (LAIR). The study is designed to obtain baseline information regarding the sequence of clinical and histopathologic events that occur in the primate foveola and cornea following exposure to a single, short duration pulse coherent light at 694.3 nm (q-switched ruby laser), 532 nm (frequency doubled neodymium laser) and 10.6 microns (carbon dioxide laser). This investigation is to be followed by a similar study in which an assessment will be made of the effects of systemic non-steroidal anti-inflammatory agents upon the extent of the laser induced lesions.

BACKGROUND

In order to provide a base upon which safety standards may be established for humans, the Division of Biorheology at LAIR has conducted a series of investigations in nonhuman subjects of the functional and morphologic effects of coherent and incoherent light upon ocular tissue. Mechanical, thermal and photochemical retinal damage is known to be produced by exposure to optic sources that produce a discrete image upon the retina at wavelengths between 400 and 1400 nm. The extent of tissue damage produced depends upon the energy level, its wavelength and its duration of exposure. Significant loss of central visual acuity may occur after a single short pulse exposure of the central portion of the retina (foveola) to laser irradiation. Because of this, ophthalmologists who use lasers to therapeutically photocoagulate lesions in the retina carefully avoid the foveola. However, inadvertent foveolar laser burns occasionally occur and these produce permanent foveolar scars. Similar foveolar burns may occur in the eyes of civilian or military personnel who are exposed to low energy laser systems either inadvertently or in battlefield situations. the extent of the retinal injury and the degree of visual loss varies with the diameter of the burn, the wavelength of the coherent light, the amplitude and duration of the incident laser energy and the individual's pupil size. Retinal burns may potentially be produced by frequency doubled neodymium sources up to a distance of 3.2 kilometers from the subject. The potential for retinal injury is enhanced when the subject is using an optical device such as a telescope or binoculars, and in such situations injury to the retina may be produced by lasers up to 10.5 kilometers distant. The total intraocular energy (TIE) necessary to have a 50% probability of causing an ophthalmoloscopically visible retinal response (ED50) has been calculated for lasers at varying wavelengths. Lasers currently used as military range finders and designators are capable of greatly exceeding ED50 dosage levels.

The deleterious effects of incident laser energy upon the retina result not only from the initial damage but also from scarring related to the associated inflammatory response. The clinical sequence of events following photocoagulation of extrafoveal retina is well known but these events have not been documented with sequential morphologic (light and electron microscopic) observations nor have these studies been performed when the

foveola is photocoagulated. Clinically within an hour after extrafoveolar photocoagulation, a white spot becomes visible. During the next three or four days the spot enlarges and appears inflamed and edematous obscuring the underlying pigment epithelium. Over the next two to three weeks, the edema and inflammation subside permitting observation of the deeper retinal layers and the retinal pigment epithelium which exhibits focal loss of pigmentation with pigment migration and clumping. The extent of the definitive scar is usually apparent within three to four weeks. There is qualitative clinical evidence suggesting that the extent of the tissue response to laser energy may be reduced by the use of systemic non-steroidal anti-inflammatory agents. Serial fluorescein angiograms have shown significant reduction in fluorescein leakage from laser induced retinal lesions after the animal was treated with systemic Indocin (5 mg/kg). This has not been documented histopathologically.

Corneal burns may be produced by lasers with wavelengths in the far infrared range. It has been shown that a single 100 nanosecond exposure to carbon dioxide laser irradiation can produce a significant central corneal opacity shortly after exposure. The precise sequence of events following infrared laser injury to the cornea has not been histologically documented. It is also not known whether or not systemic non-steroidal anti-inflammatory agents taken before and shortly after exposure will alter the extent of the eventual corneal scar.

SCOPE OF WORK

In the first year of this contract progress has been slowed by recent modifications in regulations concerning the use of animals for research purposes. An animal use protocol has now been submitted to, and approved by, the protocol review and animal use committees at Letterman Army Institute of Research. Permission to proceed with this study has been granted by the commanding officer. A firm schedule for animal exposure to coherent light has been established in consultation with personnel at LAIR. These studies will commence 16 April 1984. Initial fixation and embedding of tissue for light and electron microscopic study will begin the same day.

A microcomputer image analyzer with digitizing tablet has been designed, purchased and deliver to PPMC. The device is in working order. It will enable the area and volume of the retinal and corneal lesions to be precisely measured and recorded.

The scanning electron microscope at Lawrence Berkeley Laboratory has been prepared for use by the contractor and a utilization schedule has been provided to the contractor by personnel at LBL.

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